Docket No.: 396542

REMARKS

Restriction

The Office finds that claims 3-14 stand withdrawn because Applicant elected claims 1-2 without traverse in a prior office action. In actuality, the office action of April 18, 2003 did not request Applicant to make an election and Applicant has continued to argue these claims. Page 2 of that paper says that "claims 1-2 have been constructively elected." The Office finds that since the claims are to methods they cannot be examined, as the proper vehicle for examination would have been a divisional filing from the original prosecution. Applicant's attorney respectfully disagrees and traverses this constructive restriction for the reasons explained below.

Applicant disagrees with the Examiner's statement that election was made without traverse. Applicant previously traversed the requirement—at least by keeping the claims in prosecution in the prior response, arguing the claims and not indicating the claims were withdrawn. Applicant was never given a chance or invited to elect anything. The Examiner merely deemed this to be constructively done. Applicant continues to traverse the restriction.

This restriction is based upon a false assumption that Applicant is trying to recapture subject matter that was cancelled from the parent case. The Examiner's statements are untrue that method claims were canceled form the parent because they were not available for examination. This is a divisional of US 5,800,837, and the canceled claims are those that issued in the '837 patent. Those issued claims contain both method and product claims. The product and method claims to of the '837 patent issued together because the product was generic to the method. Those product and method both use the same chemical composition, just as the current product and method claims use the same chemical composition. Restriction is improper because the product claims are generic to the method.

The present claims were filed as a divisional because they pertain to a different chemical formula. Method claims to the use of this particular formula were never canceled from the parent. It is proper to include both method and product claims in

the present application because the product claims are generic. To emphasize this point, claims 3, 6, 9, and 12 have been amended to depend from claim 1, and this would not be possible if the product claims 1-2 were not generic to the method.

For the above reasons, Applicant respectfully asks that the restriction be withdrawn.

Specification – Amendment

The Office argues that the requested amendments to the Specification are properly correctable by certificate of correction, but finds that this type of correction is not properly submitted in reissue. Applicant's attorney respectfully traverses this basis for refusal to enter. Reissue is proper so long as there is at least one basis that supports reissue under 37 CFR 1.175. So long as this is the case, Applicant is entitled to correct other errors by either reissue or certificate of correction.

Additionally, the error sought to be corrected has already caused confusion because "alkinyl" is a foreign spelling of "alkynyl." At least 2593 issued US patents use this word, dominantly in the case of applications having foreign inventors or in the case of PCT translations. The word is always used in context of alkynyl. Applicant has amended the specification to correct this as an error, and the claims repeat this word. The claims are arguably confusing if the failure to translate this word causes confusion, and so correction is proper even in reissue.

Therefore, Applicant again requests entry of this amendment, which now does recite the entire paragraph of the parent application. In particular, the chemical formula found at column 8, lines 27-35 of U.S. Patent No. 5,997,910 has been amended to correctly change the "2" in the upper R constituent from a superscript to a subscript and the bond between that R and the P has been changed from a double bond to a single bond. This amendment corrects typographical errors in the chemical formula only, and does not add any new matter.

Claim 1 - Correction

Claim 1 has been amended to change "growth stimulating amounts . . ." in the preamble to "growth stimulating effective amounts . . ." This amendment presents no new matter. The amendment conforms reissue application claim 1 to claim 1 of the patent for which reissue is sought. The word was omitted in error during preparation of the preliminary amendment in this reissue proceeding.

Claims 1, 2 – 35 U.S.C. §112 Second Paragraph Rejection

Claims 1 and 2 stand rejected under 35 U.S.C. §112 second paragraph. In one instance of this, the Examiner has refused to enter the amendment to the specification and so finds that "alkynyl" has no support. Applicant's attorney has already explained above why the amendment to the specification is properly entered, and so asks for reconsideration and withdrawal of this rejection commensurate with entry of that amendment. Besides, "alkinyl" means "alkynyl" in at least 2593 issued US patents, and this is substantial evidence that "alkinyl" is understood as such from the perspective of ordinary skill. Therefore, "alkynyl" does find support in the parent application even if the Examiner continues to refuse entry of the amendment to the Specification.

Claim 1 also stands rejected for use of the term "in vivo fertilizer," which the Examiner finds does not meet the written description requirement because the Specification does not support use of this term. It is well accepted at law that a patent specification need not provide *in ipsis verbis* support for what is claimed so long as this is understood from a perspective of skill. The term "*in vivo*" is widely accepted as meaning in a living organism, as opposed to "*in vitro*" which means in an artificial environment outside a living organism. Claims 1 and 2 have been amended to address the type of use, which is to fertilize plants as the in vivo organism. As shown in Examples 1-5, the composition and method are useful on plants. This amendment cures any arguable problems with the language.

Claims 1-2 - 35 U.S.C. § 102(b) Rejections

The Office maintains the rejections of record with respect to Fenn, Dolan and Griffith. These references merely report investigational use of phosphonates with phosphates at extremely dilute concentrations that do not constitute what is now

claimed as "enhanced growth stimulating effective amounts." Typically, these references use concentrations in the range of 10 µm or less of either phosphate or phosphonate. This is far below the 0.25% v/v or 0.5% v/v (preferred) range shown in column 9 at lines 44-46 of US 5,997,910. It is specifically below the 0.25% to 5% range of claim 1.

The Office has dismissed without comment Applicant's previous remarks concerning the doctrine of accidental anticipation. This is indeed the same type of situation as was encountered in *Tilghman v. Proctor*, 102 U.S. 707 (1880). Tilghman's patent claimed a process of treating fats and oils by separation into fat acids and glycerin through the action of water at a high temperature and pressure. Id. at 708. Although the same separation incidentally occurred in several other prior processes, the Supreme Court rejected the notion that this prior art anticipated the patent:

> What the process was by which it was generated or formed was never fully understood. Those engaged in the art of making candles, or in any other art in which fat acids are desirable, certainly never derived the least hint from this accidental phenomenon in regard to any practicable process for manufacturing such acids.

The Federal Circuit recently affirmed this aspect of *Tilghman in Schering Corp. v. Geneva Pharms., Inc.*, 339 F.3d 1373, 1378 A reference must inevitably result is what is claimed or it is speculative and nonenabling. Applicant's attorney specifically asks the Examiner to consider this legal precedent in light of what the references show according to the following remarks.

It is speculative and untrue to say that Fenn, Dolan or Griffith teach the claimed "effective amounts." Fenn shows exactly the opposite of what the Examiner applies it to show. Fenn reports that different fungi were grown on Ribiero's medium containing 69 µg/ml Phosphonic Acid and supplemented with 100-fold increases of phosphate concentrations to assess its effect of on the percent inhibition of fungal growth produced by the fungicidal activity of phosphonic acid:

Docket No.: 396542

TABLE 4. Percentage growth inhibition of various fungi on Ribeiro's synthetic agar medium (RMSM) containing 0.84 mM H_3PO_3 (69 μg/ml) at three phosphate concentrations

Fungus	Percentage inhibition of radial growth[a] at KH_2PO_4 concentrations (mM) of:		
	0.084	0.84	8.4
Phytophthora cinnamomi (Po356)	100 a	93 a	90 a
Pythium aphanidermatum	53 b	56 b	31 b
Rhizopus stolonifer	52 b	30 c	0 c
Fusarium oxysporum f. sp. *apii*	42 b	5 d	1 c
Verticillium dahliae	49 b	0 d	1 c
Schizophyllum commune	38 b	0 e	2 c
Rhizoctonia solani	3 c	0 e	0 c

[a]Percentage based on colony growth on identical medium without H_3PO_3. Values are means of four or five replications. At a particular KH_2PO_4 concentration, values with the same letter are not significantly different according to Duncan's multiple range test ($P = 0.05$).

In each case, increasing the phosphate concentration in the presence of phosphonic acid reduced the percent of inhibition. This was true of all seven genera of fungus as well as *Phytophthora cinnamomi*, where even the addition of 100X more phosphate diminished the reported inhibition from 100% to 90%. Fenn does not show effective amounts.

Dolan presents data using similar concentrations where tomato seedlings were inoculated with *Phytophthora palmivora* to assess the effects of increasing phosphate content upon fungal infection rate. The relevant results are shown in Dolan's Table 4:

Docket No.: 396542

TABLE 4. Effect of 1 or 10 mM potassium phosphate levels on the percent inhibition of infection of tomato seedlings treated with phosphorous acid (H_3PO_3) or fosetyl-Na and inoculated with either the parental isolate of *Phytophthora palmivora* (PO376) or a mutant strain (L3) exhibiting high resistance to H_3PO_3

Treatment (PO_3 meq/L)[a]	Phosphate level (mM)	Percent inhibition of infection[b]			
		PO376		L3	
		H_3PO_3	Fosetyl-Na	H_3PO_3	Fosetyl-Na
0.85	0	57 d	6 g	17 f	0 c
2.43		100 a	36 e	59 c	0 c
6.10		100 a	100 a	71 b	2 c
0.85	1	72 c	19 f	39 e	3 c
2.43		100 a	42 d	48 d	4 c
6.10		100 a	99 a	73 b	3 c
0.85	10	87 b	69 c	45 de	39 b
2.43		100 a	91 b	75 b	45 a
6.10		100 a	100 a	82 a	45 a

[b] Bare-rooted seedlings were placed in solutions of H_3PO_3 and of fosetyl-Na with 0, 1, or 10 mM potassium phosphate buffer and inoculated immediately with zoospores. Four days after inoculation, the stem of each seedling was plated in 0.5-cm segments on PARP medium to determine percent infection. Values with the same letter are not significantly different according to Duncan's multiple range test ($P = 0.05$).

[a] Values for PO_3 meq/L were determined by dividing micrograms per milliliter by the conversion factors: 82 (H_3PO_3) or 132 (fosetyl-Na).

These results seem to controvert Fenn's Table 4, specifically, by showing that the addition of phosphate improves inhibitionagainst *P. palmivora*. Dolan noted this discrepancy with the results obtained from the similar study by Fenn, concluding on page 977 only that more research is warranted:

> The enhanced level of control of *P. palmivora* in vivo in the presence of increasing levels of phosphate was unexpected. It contradicted findings obtained with the interaction between *P. cinnamomi* and *Persea indicia*, where phosphate was shown to reduce the efficacy of both compounds [here citing the work by Fenn and Coffey]. This indicates that phosphate influence on host and fungal metabolism may be an important factor affecting the efficacy of phosphonate fungicides. The relationship between phosphate concentration in tissues host parasite metabolism, and the mode of action of phosphonate fungicides could be complex. *There is need for additional research in this area to clarify the role of the host in these interactions* [emphasis added].

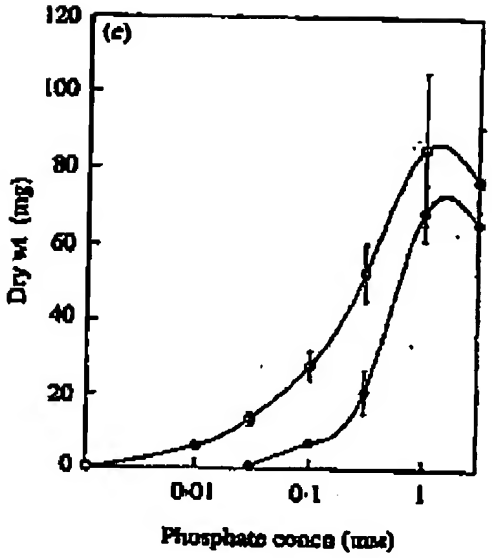
Therefore, the Examiner's own references admit that they did not understand the phenomenon and could not reproduce prior results, so more research was

warranted. These are speculative or nonenabling references, especially where the claimed "effective amounts" are significantly above what Fenn and Dolan actually used.

Griffith explains why Fenn and Dolan contradict one another. J. M. Griffith, M.D. Coffey, and B.R. Grant 1993, "Phosphonate inhibition as a function of phosphate concentration in isolates of *Phytophthora palmivora*," J. OF GENERAL MICROBIOL., 139: 2109-2116 (Griffith, Coffey &Grant) cites both Fenn and Dolan. Griffith's results came from the same *P. palmivora* organism that was also the subject of the Dolan work.

The Griffith research methods grew *P. palmivora* on medium that was enriched with phosphate at concentrations ranging up to a maximum of 1 mM. A "control" was performed for each phosphate concentration, and growth of these populations at each concentration were compared to growth on media that was also enriched with 1 mM phosphonate. These are extremely dilute concentrations of phosphate and phosphonate. Fig. 3 of Griffith, Coffey & Grant shows that the relative inhibition effect which is caused by combining phosphonate with phosphate diminishes towards 1 mM. Griffith also discusses Fig. 1(c) with regard to a mutant *P. palmivora* strain that is resistant to phosphonate, where Fig. 1(c) is replicated below:

Docket No.: 396542



The Examiner can see from the above figure that the observed inhibitory effect for which he cites Fenn, Dolan and Griffith diminishes above 1 mM. These concentrations are not useful in the real world on "in vivo" plants outside of the laboratory. Griffith states in the discussion of Fig. 1c on page 2112 (discussing isolate P7228):

> However, at higher levels of phosphonate (0.3 mM and above) phosphonate was less inhibitory to growth, and resistance to the effects of this anion was clearly demonstrated.

The overall trend as to the diminishing inhibition effect with increasing phosphate content is true with respect for all isolates in the Griffin study, which says on page 2113 that the upper limits for the observed effect were in the range of from 1 mM to 3 mM:

> However, when Pi_e (phosphate content in the media) did not limit growth, at 1 mM and 3 mM, the P376 and P7228 strains accumulated more Pi (internal phosphate content in the cells) . . . than P113)

It will be appreciated that the P376 strain is one of the two mutant strains resistant to phosphonates that Dolan investigated, and that Griffith reports a much more thorough investigation. In Dolan, the levels of phosphate and phosphonate used

Docket No.: 396542

were 10 mM and lower, which are also well below the concentrations that are now claimed.

Other work by Griffith shows that the metabolic interaction is more complex than one might otherwise imagine. The following Table is copied from J.M Griffith, R. H. Smillie, J.O. Niere and B. R. Grant, 1989 Effect of phosphate on the toxicity of phosphonate in *Phytophthora palmivora*, ARCH. MICROBIOL 152:425-429

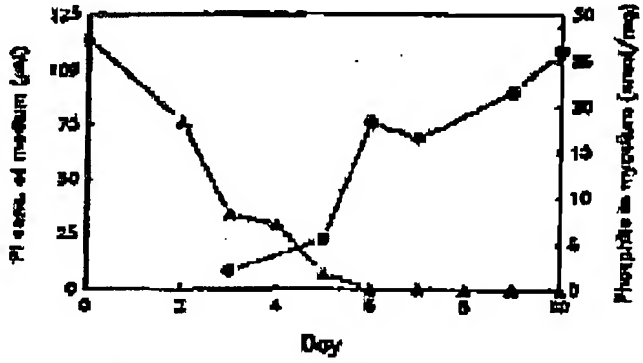


Fig. 1. The uptake of phosphite and the utilization of P_i by *Phytophthora palmivora* during growth in LPR medium containing 1 mM phosphite. P_i and phosphite concentrations were determined by ion chromatography as described in Methods. P_i in medium (▲——▲); phosphite in mycelium (●——●)

Griffith explains the significance of Fig. 1:

> Analysis of the phosphite [phosphonate] content of the mycellium grown in LPR medium in the presence of 1 mM phosphite (the concentration used by Fenn and Coffey in q1984) showed that there was an abrupt increase in the level of phosphite entering the mycellium after Pi [phosphate] had been depleted from the medium at day 6 (Fig. 1).

This is shown above in Fig. 1 where the curve on the left hand side represents diminishing phosphate content in the growth medium, and the curve on the right hand side represents phosphonate that has entered the fungal cells of *P. palmivora*. At these concentrations, the phosphonate does not start to work until the phosphate is

depleted. This explains, for example, why "[p]hosphates have also been considered to be a competitive inhibitor for phosphonate assimilation, thus inhibiting the ability of phosphonates to protect against fungus attack." U.S. 5,997,910, column 2, lines 57-60. But this is presented as a basis in support of patentability where the art shows generally that phosphates should not be mixed with phosphonates to achieve an antifungal effect.

Applicant has discovered that higher concentrations according to the claimed "effective amounts" produce an effect that differs in kind from what Fenn, Dolan and Griffith did. The art teaches away from use of the higher concentrations that are presently claimed.

For the above reasons, Applicant's attorney respectfully submits that the claims are worthy of allowance.

Applicant believes no additional fees are due, however, if any additional fee is deemed necessary in connection with this Amendment and Response, please charge Deposit Account No. 12–0600.

Respectfully submitted

Dan Cleveland, Jr. Reg. No. 36,106
Lathrop & Gage L.C.
4845 Pearl East Circle, Suite 300
Boulder, CO 80301
(720) 391-3012 (phone)
(720) 931-3001 (fax)